REMARKS

I. Status of the Claims

Upon entry of the amendment claims 119 and 127 are pending. Claim 119 is amended herewith. Support for the amendment is to claim 119 is replete in the specification including, e.g., page 43, lines 8-9 and page 116, line 19 to page 117, line 24. Claim 127 is withdrawn from consideration as directed to a non-elected invention. The amendment or cancellation of claims is made without prejudice to future prosecution.

II. Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 121-126 were rejected as allegedly introducing new matter. Applicants disagree, and respectfully submit these claims are fully supported in the specification as filed. However, to expedite prosecution Applicants have cancelled these claims. The cancellation is without prejudice to prosecuting claims directed to this subject matter in this or a related application.

Claims 119-126 were rejected as allegedly not enabled by the specification. This rejection is moot as it applies to claims 120-126. Applicants respectfully traverse this rejection as it applies to claim 119.

The bases for the rejection of these claims are, as Applicants understand them from pages 6-12 of the Office Action:

- Allegedly one of skill could not obtain a representative number of polynucleotides falling within the claim without undue experimentation. This is in part because "the claims are drawn broadly to a very large genus of polynucleotides . . .".
- Allegedly the specification provides insufficient guidance to enable the skilled artisan to determine which alterations in any TRT can be made without altering the functional properties of the encoded protein, in part because even a single conservative amino acid substitution can adversely affect biological activity.

Applicants will address each of these bases in turn.

No undue experimentation is required to make the claimed polynucleotides

The instant claims are directed to polynucleotides encoding a protein defined by structure (a degree of identity to a reference protein and the presence of six amino acid motifs identified by the inventors) and function (an assayable activity). Applicants respectfully submit the specification provides both the prototype sequence and activity assays, and clearly enables one of ordinary skill to make active variants without undue experimentation. It appears Applicants and the Office are in agreement that the specification enables assays for telomerase activity and methods of mutagenesis of nucleic acids (see Office Action mailed April 9, 2004, at page 9). Further, it is not disputed the specification provides the reference sequence (SEQ ID NO:118) and teaches the TRT motifs recited in claim 119. Applicants submit one with knowledge of the instant specification could, using only routine molecular biology techniques, introduce mutations into SEQ ID NO:118 while retaining the TRT motifs or otherwise identify a nucleic acid encoding a protein at least 60% identical to SEQ ID NO:118 and containing the TRT motifs. One of ordinary skill with knowledge of the instant specification would be able to identify those encoded proteins having telomerase activity. Numerous mutation strategies were know to scientists at the time the claimed invention was made. The standard texts *Protocols in Molecular Biology* (Ausubel et al. eds.) and *Molecular Cloning: A Laboratory Manual* (Sambrook et al. eds.) describe techniques employing chemical mutagenesis, cassette mutagenesis, degenerate oligonucleotides, mutually priming oligonucleotides, linker-scanning mutagenesis, alanine-scanning mutagenesis, and error-prone PCR. Other efficient methods include the *E. coli* mutator strains of Stratagene (Greener et al., Methods Mol. Biol. 57:375, 1996) and the DNA shuffling technique described by W.P.C. Stemmer (*Proc. Natl. Acad. Sci. USA* 91:10747, 1994; and *Nature* 370:389, 1994; also see Patten et al., *Curr. Opin. Biotechnol.* 8:724, 1997). Using the DNA shuffling technique, the encoding regions are fragmented, annealed under low stringency conditions, and then amplified by PCR. These methods can be used to create variants, the amplified DNA would next be introduced into a an expression cassette (described in the specification at, *e.g.*, pages 168-200), and then transfected into *E. coli,* thereby producing a library of thousands of variant TRT cDNAs. In view of the known variability of naturally occurring TRT sequences, a substantial proportion of the artificial variants would be expected to

retain telomerase activity. Applicants submit it would not be unduly burdensome to construct a library of thousands of TRT variants based on the reference sequence, using any one of several techniques known in the art at the time this application was filed. The library could then be easily screened using assays described in the specification to identify variants with telomerase activity.

The Office has recognized that a claimed genus of polynucleotides can be properly defined by reference to a prototype sequence and an activity of an encoded protein, and the Office commonly grants claims in which a claimed polynucleotide is defined by structure and function. For example, in a recent decision, the Board of Patent Appeals and Interferences found that a claim for a polynucleotide having at least 80% sequence identity to a prototype sequence (An isolated . . . wee1 polynucleotide having at least 80% sequence identity to the entire coding region of SEQ ID NO:1 . . .) was both described and enabled. *Ex parte Yuejin Sun et al.* (BPAI 2003, Appeal No. 2003-1993; copy enclosed). Although this opinion was not written for publication and is not binding precedent of the Board, Applicants submit the reasoning articulated in the opinion is nonetheless useful in addressing the merits of the present case. In *Ex parte Sun*, the examiner had argued the claim was not enabled because "the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" and the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in alteration of the plant's phenotype." The Board reversed the rejection, observing that the specification provided the chemical *structure* of a polynucleotide that comprises the coding sequence set forth in SEQ ID NO:1, provided an example of *how to screen* for WEE1 activity, and observed that "most of the variations in the amino acid sequence of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. *In the present case, the specification provides the "chemical structure" of the reference sequence, describes assay methods, and* not only *provides guidance as to which regions from the TRT protein are*

conserved, but requires *in the claim that the motifs be present in the claimed variants.* Applicants submit the presently claimed invention is enabled by the guidance found in the specification.

Further, Applicants believe the Office has not established that it would require undue experimentation to make and use the variants using the methods suggested by the Applicants. Rather, the Office takes the position, as Applicants understand it, that the genus encompassed by the claims is so large that "screening all natural and non-natural variants of TRT . . . is not considered routine." First, this seems to focus on the *number* of variants to be screened. As the CAFC has noted, a considerable amount of screening (*e.g.*, screening numerous hybridomas for monoclonal antibodies) is not necessarily *undue* experimentation. Second, Applicants submit that screening all variants is not the proper measure of enablement. Many issued claims to chemical compounds, for example, call out structures in which various constituents are defined by R groups. These claims can encompass a large number of compounds. Given the nature of organic synthesis it could take considerable effort (if even possible) to make all members of the genus. This does not render such claims not enabled. Similarly, as noted above, numerous issued and presumptively enabled patents include claims to polynucleotides defined by percent identity to a reference sequence and a biological activity. In some cases it might take considerable effort to make each and every polynucleotides in the genus but, again, this does not render such claims not enabled.

The specification provides sufficient guidance for making variants

The Office also asserted that the specification provides insufficient guidance for making variants, in part because even a single conservative amino acid substitution can adversely affect biological activity. It is no doubt true that in some proteins even a single conservative amino acid substitution at a catalytic site can adversely affect biological activity. It is equally true, however, that in many proteins *most* substitutions do not eliminate activity and many substitutions can increase activity. In the case of the subject matter of this application, telomerase reverse transcriptase, the instant specification provides striking evidence that a ***considerable amount of variation*** is tolerated in catalytically active telomerase proteins. The

specification describes the sequences of six telomerase proteins, with highly diverse sequences. Mouse TRT, for example, has only about 64% identity to human TRT and TRT sequences in different eukaryotes can have identities of less than 30%, and yet perform essentially the same function. One of skill in the art would ascertain from this teaching that a wide range of substitutions, deletions, etc. would be tolerated while retaining activity, provided the characteristic motifs are present.

Further, the specification provides ample guidance to one of ordinary skill in the art, e.g., a molecular biologist or protein chemist, for making variants. The application provides an extensive comparison of sequences: One skilled in the art would recognize that alterations to non-conserved regions would less likely adversely affect activity as compared to alterations in conserved regions. The specification teaches in detail that telomerases share common features in the form of structural motifs, which motifs are described in detail. The specification also describes examples of a variety of conservative substitutions that could be made that would have a higher likelihood of not disrupting the activity of the encoded protein (see, e.g., page 113, line to page 114, line 19). The Office has referred to only a single example of a variant not having telomerase catalytic activity, the 182-bp deletion variant *lacking* the motifs required by the claim and *identified* in the specification not having telomerase catalytic activity.

Applicants have provided several examples of TRT proteins with diverse sequences, demonstrating a considerable amount of variation is tolerated in catalytically active telomerase proteins. Applicants have described the motifs that characterize catalytically active telomerase proteins and has claimed polynucleotides with reference to both function and structure, *including the presence of the mofits* which are recited in the pending claim. The skilled artisan using routine molecular biological techniques and assays taught in the specification could make and use the claimed polynucleotides. The enablement requirement of Section 112 does not require more. For these reasons, Applicants respectfully submit this rejection should be withdrawn.

III. Claim Rejections under 35 USC 112, Second Paragraph

Claims 121-126 were rejected as allegedly indefinite. This rejection is now moot in view of the cancellation without prejudice of these claims.

IV. Claim Rejections under 35 USC 102(e)

Claims 119-126 were rejected as anticipated under 35 USC 102(e) by U.S. Pat. No. 6,093,809 and U.S. Pat. No. 6,309,867 (each having the same specification). These patents disclose the TRT proteins of Euplotes aediculatus, Schizaromyces, Saccharomyces and human. Of these, the Euplotes, Schizaromyces, and Saccharomyces proteins cannot anticipate claim 119, because none is at least 60% identical to SEQ. ID NO:118 when the entire sequence of said protein is optimally aligned with SEQ ID NO:118. The maximal amino acid identity for the most closely matched subsequences is approximately 21%, 21% and 25%, respectively, between SEQ ID NO:118 and *Euplotes aedicaulatus*, *Schizosccharomyces pombe*, and *Saccharomyces cerevisiae* proteins.[1]

SEQ ID NO:118 is the human TRT sequence. The human TRT sequence is disclosed and claimed in US Pat. No. 6,309,867, having the same inventorship as the instant application. Accordingly Applicants submit the disclosure of human TRT in U.S. Pat. No. 6,093,809 and U.S. Pat. No. 6,309,867 is not "by another" as required by 102(e).

V. Claim Rejections under 35 USC 102(a)

Claim 119 was rejected under 35 USC 102(a) in view of either Lingner (describing p123 of *Euplotes*) or Lendvay (describing EST2 of *S. cerevisiae*). However, neither reference described nucleic acids encoding a polypeptide with at least 60% sequence identity to SEQ ID NO:118. For this reason, neither reference anticipated the present invention.

VI. Claim Rejections under Obviousness Type Double Patenting

Claims 119-126 were rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 3, 4 and 7-10 of U.S. Patent No. 6,261,836. Applicants will file

[1]BLAST alignments of the sequences are provided in the Appendix to this response. Alignments of only portions of the TRT sequences are aligned (the level of sequence identity in other regions apparently is too low for any meaningful alignment and inclusion of these regions would result in a *lower* percentage of identity). In the case of the *Schizosccharomyces pombe* sequence, two different regions are aligned (having sequence identities of 23% and 25%.)

a terminal disclaimer or take other appropriate action upon indication that the application is otherwise in condition for allowance.

Claims 119-126 were rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 3, 4 and 7-10 of U.S. Patent No. 6,093,809. The Office states the present claims are drawn to polynucleotides encompassed by the genus now claimed. The '809 patent disclosed the TRT sequences for *Euplotes aedicaulatus* and *S. cerevisiae*. As explained above Applicants have previously explained that these sequences share little identify with SEQ ID NO:118 and are not encompassed by the instant claims. Accordingly, it is requested that this rejection be withdrawn.

Claims 119-126 were rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,767,719, which describes mouse TRT. The Office correctly asserts that the polynucleotides of the '719 patent are encompassed by claim 119. The Office argues that the polynucleotides claimed in the '719 patent anticipate the instantly claimed polynucleotides (as a species anticipates a genus) and thus render the instant claims obvious.

Using the one-way test for obviousness to determine whether a double-patenting rejection is appropriate, the question is whether the polynucleotides of the '719 patent (encoding mouse TRT) are an *obvious variant* of the polynucleotides claimed in the instant application. Applicants submit the "mouse" TRT polynucleotides of the '719 patent are not an obvious variant of the claimed polynucleotides. That is, one apprised of the pending generic claims would not find the specific mouse sequence obvious. Thus, under the one-way obviousness test, no double-patenting rejection is appropriate. In determining whether a one-way or two-way obviousness test is used, the MPEP discusses two situations in which double patenting between a patent and an application might occur, *i.e.*, when the filing date of the patent is later than the application and when the filing date of the patent is earlier than the application. *Neither* situation is present here, as the instant application and the application underlying the '719 patent both were filed on November 19, 1997. The Applicant could not have prosecuted the claims in a single application because they are separately owned. Both applications were diligently prosecuted and concurrently prosecuted. Further, issuance of a patent from the instant application will not result

in patent term beyond the expiration of the '719 patent. For these reasons, this double patenting rejection should be withdrawn.

VII. Rejoinder of Claim 127

Claim 127 is directed to a method of increasing proliferative capacity in vitro. Claim 127 is a method claim that depends and incorporates the limitations of product claim 119. Accordingly, upon establishing that claim 119 is free of prior art, then claim 127 will also be free of prior art. For this reason, applicants request that claim 127 be rejoined into the group under examination, in accordance with MPEP § 821.04.

CONCLUSION

Applicants respectfully request that all rejections be reconsidered and withdrawn.

Respectfully submitted,

Date: September 8, 2005

Randolph T. Apple
Reg. No. 36,429

Appendix: Sequence Alignments

Enclosure: *Ex parte Sun et al.*

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San Francisco, California 94111-3834
Tel: 303-571-4000
Fax: 415-576-0300

60580657 v1

APPENDIX

015389-002950US

Blast 2 Sequences results

PubMed Entrez BLAST OMIM Taxonomy Structure

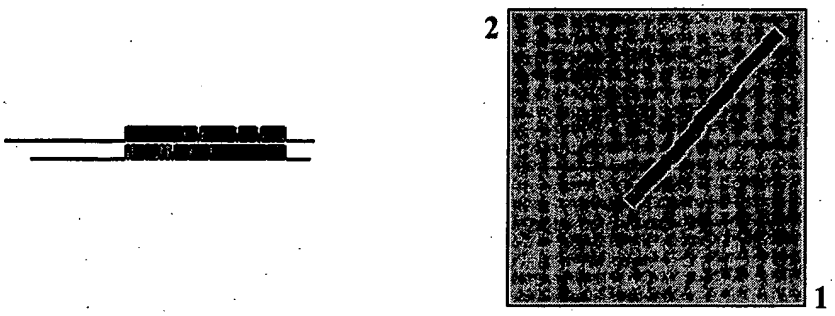
Query: Human
vs.
Subject: *Euplotes*

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.10 [Oct-19-2004]

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter Align

Sequence 1 lcl|seq_1 **Length** 1126 (1 .. 1126)

Sequence 2 lcl|seq_2 **Length** 1031 (1 .. 1031)



NOTE:The statistics (bitscore and expect value) is calculated based on the size of nr database

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            F+      ++P      R N + F +  KK++ L KH  +    L  K++ R+ +W++
Sbjct: 361  FINEFFYNILPKDFLTGR-NRKNFQKKVKKYVELNKHELIHKNLLLEKINTREISWMQVE 419

Query: 520  PGVGCVPAAEHRLREEILAKFLHWLMSVYVVELLRSFFYVTETTFQKNRLFFYRKSVWSK 579
                      +H     +L K L W+    VV L+R FFYVTE     ++ ++YRK++W
Sbjct: 420  TSAKHFYYFDHE-NIYVLWKLLRWIFEDLVVSLIRCFFYVTEQQKSYSKTYYYRKNIWDV 478

Query: 580  LQSIGIRQHLKRVQLRELSEAEVRQHREARPALLTSRLRFIPKPDGLRPIVNMDYVVGAR 639
            +  + I   LK+  L E+ E EV + +++       +LR IPK    RPI+  +     +
Sbjct: 479  IMKMSIAD-LKKETLAEVQEKEVEEWKKSL-GFAPGKLRLIPKKTTFRPIMTFN----KK 532

Query: 640  TFRREKRAERLTSRVKALFSVLNYERARR---PGLLGASVLGLDDIHRAWRTFVLRVRAQ 696
                +++  +LT+  K L S L  +  +        G +V   DD+ + + + FV + + Q
Sbjct: 533  IVNSDRKTTKLTTNTKLLNSHLMLKTLKNRMFKDPFGFAVFNYDDVMKKYEEFVCKWK-Q 591

Query: 697  DPPPELYFVKVDVTGAYDTIPQDRLTEVI--------------ASIIKPQNTYCVRRYAV 742
               P+L+F  +D+   YD++ +++L+  +               A I+K +N   +
Sbjct: 592  VGQPKLFFATMDIEKCYDSVNREKLSTFLKTTKLLSSDFWIMTAQILKRKNNIVIDSKNF 651

Query: 743  VQKAAHGHVRKAFKSHVSTLTDLQPYMRQFVAHLQETSPLRDAVVIEQSSSLNEASSGLF 802
             +K    + R+ F+  ++      P +   + + Q     +  +++E           L
Sbjct: 652  RKKEMKDYFRQKFQK-IALEGGQYPTLFSVLENEQNDLNAKKTLIVEAKQRNYFKKDNLL 710

Query: 803  DVFLRFMCHHAVRIRGKSYVQCQGIPQGSILSTLLCSLCYGDMENKLFAGIRRD------ 856
               +    ++ +   GK Y Q +GIPQG  +S++L S   Y  +E      +R +
```

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Sbjct: 711  QPVINICQYNYINFNGKFYKQTKGIPQGLCVSSILSSFYYATLEESSLGFLRDESMNPEN 770

Query: 857  ---GLLLRLVDDFLLVTPHLTHAKTFLRTLVRGVPEYGCVVNLRKTVVNFPVEDEALGGT 913
             LL+RL DD+LL+T    +A  F+  L+    E G   N++K   +FP+
Sbjct: 771  PNVNLLMRLTDDYLLITTQENNAVLFIEKLINVSRENGFKFNMKKLQTSFPLSPSKFAKY 830

Query: 914  AFVQMPAHGLF----PWCGLLLDTRTLEVQSDYSSYARTSIRASLTFNRGFKAGRNMRRK 969
             +    +      W G+ +D +TL +  + +      I  +L  N   K      +K
Sbjct: 831  GMDSVEEQNIVQDYCDWIGISIDMKTLALMPNINLRIE-GILCTLNLNMQTKKASMWLKK 889

Query: 970  LFGVLRLKCHSLFLDLQVNSLQTVCTNIYKILLLQAYRFHACVLQLPFH 1018
                +  + +    + +       + K+ +   Y++  C  +   H
Sbjct: 890  KLKSFLMNNITHYFRKTITTEDFANKTLNKLFISGGYKYMQCAKEYKDH 938

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Gapped
Lambda     K      H
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Gap Penalties: Existence: 11, Extension: 1
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Number of successful extensions: 7
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Number of HSP's better than 10.0 without gapping: 1
Number of HSP's gapped: 2
Number of HSP's successfully gapped: 1
Number of extra gapped extensions for HSPs above 10.0: 0
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Length of database: 871,278,970
Length adjustment: 142
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Effective length of database: 871,278,828
Effective search space: 857338366752
Effective search space used: 857338366752
Neighboring words threshold: 9
Window for multiple hits: 0
X1: 15 ( 7.0 bits)
X2: 129 (49.7 bits)
X3: 129 (49.7 bits)
S1: 40 (21.6 bits)
S2: 83 (36.6 bits)
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015389-002950US

Blast 2 Sequences results

Query: Human
vs.
Subject: *Saccharomyces*

PubMed Entrez BLAST OMIM Taxonomy Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.10 [Oct-19-2004]

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter Align

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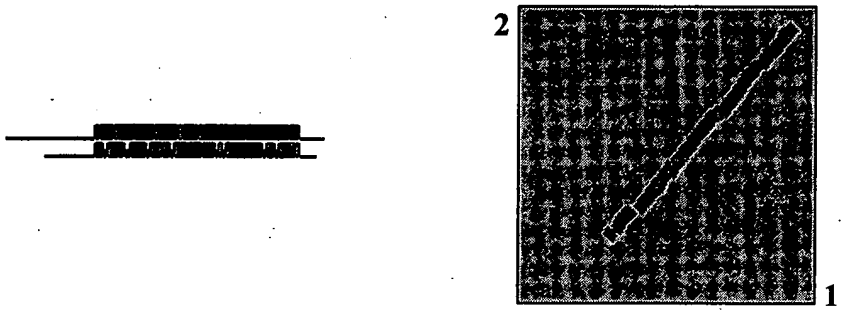
Sequence 2 lcl|seq_2 **Length** 884 (1 .. 884)



NOTE:The statistics (bitscore and expect value) is calculated based on the size of nr database

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Sbjct: 199  FPYSKILPSSSSIKKLTDLREAIF----------PTNLVKIPQRLKVRINLTLQKLLKRH 248

Query: 397  AQCPYGVLLKTHCPLRAAVTPAAGVCAREKPQGSVAAPEEEDTDPRRLVQLLRQHSSPWQ 456
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Sbjct: 249  KRLNYVSILNSICPPLEGTVLDLSHLSRQSPKE-------------------------R 282

Query: 457  VYGFVRACLRRLVPPGLWGSRHNERRFLRNTKKFISLGKHAKLSLQELTWKMSVRDCAWL 516
            V  F+   L++L+P  ++GS+ N+ + ++N    +SL  +  L    L  K+ ++D  WL
Sbjct: 283  VLKFIIVILQKLLPQEMFGSKKNKGKIIKNLNLLLSLPLNGYLPFDSLLKKLRLKDFRWL 342

Query: 517  RRSPGVGCVPAAEHRLR--EEILAKFLHWLMSVYVVELLRSFFYVTETTFQKNRLFFYRK 574
                 +  +   +H      ++   F+ WL    + +++++FFY TE +     + ++R
Sbjct: 343  -----FISDIWFTKHNFENLNQLAICFISWLFRQLIPKIIQTFFYCTEIS-STVTIVYFRH 397

Query: 575  SVWSKLQSIGIRQHLKRVQLRELSEAEV-RQHREARPALLT-SRLRFIPKPDGLRPIVNM 632
              W+KL +  I ++ K      L E  V R H     +    S++R IPK       +
Sbjct: 398  DTWNKLITPFIVEYFKTY----LVENNVCRNHNSYTLSNFNHSKMRIIPKKSNNEFRIIA 453

Query: 633  DYVVGARTFRREKRAERLTSRVKALFSVLNYERARRPGLLGA--SVLGLDDIHRAWRTFV 690
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Query: 691  LRVRAQDPPPELYFVKVDVTGAYDTIPQDRLTEVIASIIKPQNTYCVRRYAVVQKAAHGH 750
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Query: 751  VRKAFKSHVSTLTDLQPYMRQFVAHLQETSPLRDAVVIEQSSSLNEASSGLFDVFLRFMC 810
             +  F ++   L       + F        P    + I+   +++ ++  + +V    +
Sbjct: 562  -QYFFNTNTGVL-------KLFNVVNASRVPKPYELYIDNVRTVHLSNQDVINVVEMEIF 613

Query: 811  HHAVRIRGKSYVQCQGIPQGSILSTLLCSLCYGDM---ENKLFAGIRRDGLLLRLVDDFL 867
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Query: 868  LVTPHLTHAKTFLRTLVRGVPEYGCVVNLRKTVVNFPVEDEALGGTAFVQMPAHGLFPWC 927
             +++          +  + G  +Y    N  K +      D+             +  +C
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Query: 928  GLLLDTRTLEVQSDYSSYARTSIRASLTFNRGFKAGRNMRRKLFGVLRLKCHSLFLDLQV 987
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Query: 988  NSLQTVCTNIYKIL--LLQAYRFHACVLQLPFHQQVWKNPTFFLRVISDTASLC 1039
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Sbjct: 774  NSTNTVLMQIDHVVKNISECYKSAFKDLSINVTQNM-QFHSFLQRIIEMTVSGC 826
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CPU time: 0.06 user secs. 0.01 sys. secs 0.07 total secs.

Lambda	K	H
0.324	0.138	0.435

Gapped

Lambda	K	H
0.267	0.0410	0.140

Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Sequences: 1
Number of Hits to DB: 5476
Number of extensions: 3844
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Number of HSP's better than 10.0 without gapping: 1
Number of HSP's gapped: 1
Number of HSP's successfully gapped: 1
Number of extra gapped extensions for HSPs above 10.0: 0
Length of query: 1126
Length of database: 871,278,970
Length adjustment: 142
Effective length of query: 984
Effective length of database: 871,278,828
Effective search space: 857338366752
Effective search space used: 857338366752
Neighboring words threshold: 9
Window for multiple hits: 0
X1: 15 (7.0 bits)
X2: 129 (49.7 bits)
X3: 129 (49.7 bits)
S1: 40 (21.6 bits)
S2: 83 (36.6 bits)

015389-002950US

Blast 2 Sequences results

Query: Human
vs.
Subject: *Schizosaccharomyces*

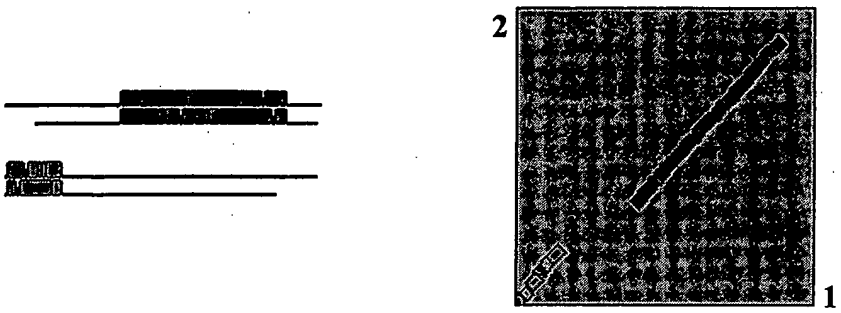
PubMed Entrez BLAST OMIM Taxonomy Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.10 [Oct-19-2004]

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter Align

Sequence 1 lcl|seq_1 **Length** 1126 (1 .. 1126)

Sequence 2 lcl|seq_2 **Length** 988 (1 .. 988)



NOTE:The statistics (bitscore and expect value) is calculated based on the size of nr database

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Identities = 147/573 (25%), Positives = 276/573 (47%), Gaps = 47/573 (8%)

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            ++L     P QV+ F+R+ L R+ P  +WG++      L++ + F+ L ++   SL  L
Sbjct: 332  KILSYSLKPNQVFAFLRSILVRVFPKLIWGNQRIFEIILKDLETFLKLSRYESFSLHYLM 391

Query: 506  WKMSVRDCAWL---RRSPGVGCVPAAEHRLREEILAKFLHWLMSVYVVELLRSFFYVTET 562
              + + +  WL    +RS     C+  ++    R++I A+F++WL + +++ +L+SFFY+TE+
Sbjct: 392  SNIKISEIEWLVLGKRSNAKMCL--SDFEKRKQIFAEFIYWLYNSFIIPILQSFFYITES 449

Query: 563  TFQKNRLFFYRKSVWSKLQSIGIRQHLKRVQLRELSEAEVRQHREARPALLTSRLRFIPK 622
            +  +NR  ++RK +W KL         +K      +++E  VR   + +  L  + +R +PK
Sbjct: 450  SDLRNRTVYFRKDIW-KLLCRPFITSMKMEAFEKINENNVRMDTQ-KTTLPPAVIRLLPK 507

Query: 623  PDGLRPIVNMDYVVGARTFRREKRAERLTSRVKALFSVLNYERARRPGLLGASVLGLD-- 680
             + R I N+       +     +K         ++ + S+L +        L+      G+
Sbjct: 508  KNTFRLITNLRKRFLIKMGSNKKMLVSTNQTLRPVASILKH-------LINEESSGIPFN 560

Query: 681  -DIHRAWRTF---VLRVRAQDPPPELYFVKVDVTGAYDTIPQDRLTEVIASIIKPQNTYC 736
             +++     TF    +L+ R       + YFV++D+    YD I QD +  ++    +K     +
Sbjct: 561  LEVYMKLLTFKKDLLKHRMFG--RKKYFVRIDIKSCYDRIKQDLMFRIVKKKLKDPE-FV 617

Query: 737  VRRYAVVQKAAHGHVRKAFKSHVSTLTDLQPYMRQFVAHLQETSPLRDAVVIEQSSSLNE 796
            +R+YA +  A       K F S   +  D+ P+ +       +TS   D + ++       +
Sbjct: 618  IRKYATIH-ATSDRATKNFVSEAFSYFDMVPFEKVVQLLSMKTS---DTLFVDFVDYWTK 673

Query: 797  ASSGLFDVFLRFMCHHAVRIRGKSYVQCQGIPQGSILSTLLCSLCYGDMENKLFAGIRRD 856
            +SS +F +    +  H V+I    Y+Q  GIPQGSILS+ LC     D+ ++  +  +  ++
```

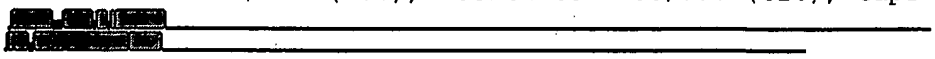
```
Sbjct: 674  SSSEIFKMLKEHLSGHIVKIGNSQYLQKVGIPQGSILSSFLCHFYMEDLIDEYLSFTKKK 733

Query: 857  G-LLLRLVDDFLLVTPHLTHAKTFLRTLVRGVPEYGCVVNLRKTVVNFPVEDEALGGTAF 915
            G +LLR+VDDFL +T +   AK FL   +RG  ++    +L KTV+NF   +  +  T F
Sbjct: 734  GSVLLRVVDDFLFITVNKKDAKKFLNLSLRGFEKHNFSTSLEKTVINFENSNGIINNTFF 793

Query: 916  VQMPAHGLFPWCGLLLDTRTLEV-----QSDYSSYARTSIRASLTFNRGFKAGRNMRRKL 970
             +       P+ G  ++ R+L+       + D + +  TS+  +    + F
Sbjct: 794  NESKKR--MPFFGFSVNMRSLDTLLACPKIDEALFNSTSVELTKHMGKSF---------F 842

Query: 971  FGVLRLKCHS---LFLDLQVNSLQTVCTNIYKI 1000
            + +LR    S   +F+D+  NS    C NIY++
Sbjct: 843  YKILRSSLASFAQVFIDITHNSKFNSCCNIYRL 875

Score = 37.0 bits (84), Expect = 6.4
Identities = 44/191 (23%), Positives = 80/191 (41%), Gaps = 30/191 (15%)
```



```
Query: 5    PRCRAVRSLLRSHYREVLPLATFVRRLGPQGWRLVQRGDPAAFRALVAQCL--------- 55
            P+ R +R  L + Y  +  L  +V+       LV RG PA+  + + + L
Sbjct: 7    PKSRILR-FLENQYVYLCTLNDYVQ--------LVLRGSPASSYSNICERLRSDVQTSFS 57

Query: 56   -----VCVPWDARPPPAAPSFRQVSCLKELVARVLQRLCERG---AKNVLAFGFALL--D 105
                 V +D++P               EL+A V++++ +      +N+L  GF++   D
Sbjct: 58   IFLHSTVVGFDSKPDEGVQFSSPKCSQSELIANVVKQMFDESFERRRNLLMKGFSMNHED 117

Query: 106  GRGPP-EAFTTSVRSYLPNTVTDALRGSGAWGLLLRRVGDDVLVHLLARCALFVLVAPSC 164
             R          + S  PN +   L     W LLL  +G D + +LL++ ++F  +
Sbjct: 118  FRAMHVNGVQNDLVSTFPNYLISILESKN-WQLLLEIIGSDAMHYLLSKGSIFEALPNDN 176

Query: 165  AYQVCGPPLYQ 175
             Q+ G PL++
Sbjct: 177  YLQISGIPLFK 187

CPU time:     0.07 user secs.       0.00 sys. secs          0.07 total secs.

Lambda     K      H
   0.324    0.138    0.435

Gapped
Lambda     K      H
   0.267   0.0410    0.140


Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Sequences: 1
Number of Hits to DB: 6168
Number of extensions: 4333
Number of successful extensions: 8
Number of sequences better than 10.0: 1
Number of HSP's better than 10.0 without gapping: 1
Number of HSP's gapped: 3
Number of HSP's successfully gapped: 2
Number of extra gapped extensions for HSPs above 10.0: 0
Length of query: 1126
Length of database: 871,278,970
Length adjustment: 142
Effective length of query: 984
```

```
Effective length of database: 871,278,828
Effective search space: 857338366752
Effective search space used: 857338366752
Neighboring words threshold: 9
Window for multiple hits: 0
X1: 15 ( 7.0 bits)
X2: 129 (49.7 bits)
X3: 129 (49.7 bits)
S1: 40 (21.6 bits)
S2: 83 (36.6 bits)
```

Paper No. 27

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte YUEJIN SUN, BRIAN R. DILKES, BRIAN A. LARKINS, KEITH S. LOWE, WILLIAM J. GORDON-KAMM and RICARDO A. DANTE

Appeal No. 2003-1993
Application No. 09/470,526

ON BRIEF

Before WILLIAM F. SMITH, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 2-11, 31, 33 and 35-36 which are the claims on appeal in this application. Claims 14, 32 and 37 have been allowed.

Claim 31 is illustrative of the claims on appeal and reads as follows:

31. An isolated wee1 nucleic acid comprising a member selected from the group consisting of:
(a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2.;
(b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;

(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and
(d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The prior art references relied upon by the examiner are:

Aligue et al. (Aligue), "Regulation of *Schizosaccharomyces pombe* Wee1 Tyrosine Kinase," J. Biol. Chem., Vol. 272, pp. 13320-13325 (1997)

Hemerly et al. (Hemerly), "Dominant negative mutants of the Cdc2 kinase uncouple cell division from iterative plant development," The EMBO Journal, Vol. 14, pp. 3925-3936 (1995)

Grounds of Rejection

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

These rejections are reversed.

DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

Background

The subject matter of the present application is generally directed to corn plant nucleic acids and their encoded proteins which are involved in cell cycle regulation. Specification, page 4. In particular, the claimed invention is directed to a wee1 homologue from maize, zmwee1, whose activity resembles related protein tyrosine kinases. Specification, page 6. The zmwee1 protein is indicated in the specification to be useful in the genetic engineering of the corn plant to increase maize productivity. Specification, page 3.

More specifically, claim 31 is directed to an isolated wee1 nucleic acid comprising a member selected from the group consisting of: a polynucleotide that encodes a polypeptide of SEQ ID NO:2.; a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1; a polynucleotide comprising the

coding sequence set forth in SEQ ID NO:1; and a polynucleotide complementary to a polynucleotide described above.

According to the prior art, Aligue, Wee1 tyrosine kinase regulates mitosis by carrying out the inhibitory tyrosine 15 phosphorylation of Cdc2 M-phase inducing kinase. Abstract. The specification confirms this, stating "induced wee1 overexpression results in phosphorylation of p34 at tyrosine-15 (inactivating p34), effectively blocking the transition from G2 into mitosis." Specification, page 37. The "encoded [wee1] protein is an important part of the checkpoint control machinery that regulates $p34^{cdc2}$ activity and it's [sic] participation in the active MPF (maturation promoting factor) complex." Specification, page 36. Wee1 activity can be stimulated by the CDK2-cyclin A complex, or inhibited by nim1. Specification, page 36.

Description

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

The Federal Circuit has discussed the application of the written description requirement of the first paragraph of § 112 to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus . . . [H]owever, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id.

The Lilly court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

The Federal Circuit has also addressed the written description requirement in the context of DNA-related inventions. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of **sufficiently detailed, relevant identifying characteristics** . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] Id. at 1324, 63 USPQ2d at 1613 .

The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines). The Guidelines apply to proteins as well as DNAs.

Finally, it is well-settled that the written description requirement of 35 U.S.C. § 112, first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. See, e.g., In re Herschler, 591 F.2d 693, 700, 200 USPQ 711, 717 (CCPA 1979): "The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including

those limitations." (citations omitted). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

We apply the relevant law above to the facts before us. In the present case, the examiner argues that the "specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids and transgenic cells, plants and seeds." Answer, page 4. The examiner argues that one skilled in the art "could not predict the structure and function of isolated nucleic acids comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 or a polynucleotide complementary thereto, or cells, plants and seeds transformed therewith. The physical features of the claimed isolated nucleic acids and transgenic cells, plants, and seeds cannot be ascertained in the absence of information about the functional activities of these nucleic acids. Additionally, the specification does not disclose the effect of incorporating the claimed isolated nucleic acids into the genome of a cell or plant." Id.

We find the examiner's argument that one skilled in the art could not predict the structure and function of isolated nucleic acids comprising a wee1 to be confusing in the context of a written description rejection, as predictability is not the legal standard or test for such rejections. However, as best we can understand the examiner's argument, the examiner appears to argue that the specification does not describe a wee1

polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

The examiner argues that "Applicant's [sic] own specification fails to teach a single representative species with 80% identity and WEE1 function." Answer, page 5.

We do not agree with the examiner that claim 31 lacks written description in the specification and that appellants were not in possession of the claimed invention at the time the application was filed. First, to satisfy the written description requirement it is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented the claimed subject matter. Thus, we do not find the fact that the specification does not specifically teach the structure of a species with 80% identity and WEE1 function to be dispositive of the written description issue here.

The Enzo court stated that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with Enzo (*supra*).

In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

The examiner relies on Aligue for the teaching that amino acids 363-408 of the 550 amino acid N-terminal regulatory domain of *S. pombe* WEE1 are critical to the function of the regulatory domain. The examiner concludes that because "the functional properties of WEE1 and other proteins reside in specific amino acid residues, changes in these residues could have an effect on WEE1 function." Answer, page 5.

We agree with appellants that the examiner has not established with a preponderance of the evidence, that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to describe a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. What is evident from the record is those of ordinary skill in the art were aware that most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. Those of skill in the art were also aware that the carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis. Thus, those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented the isolated wee1 having the specific nucleotide and amino acid sequences and variations of these sequences with mutations in described specific areas of Wee1, while avoiding the introduction of mutations in other regions. This teaching, coupled with the ability to test for functional mutants with the assays provided for in the specification, supports appellants' position that the inventors sufficiently described and were in possession of the invention as claimed, at the time of filing of the patent application.

In our view the examiner has not provided sufficient evidence or analysis to indicate why one of ordinary skill in the art having read the disclosure, would not have been able to recognize that the inventors invented the subject matter within the scope of the claims. The rejection of the claims for lack of written description is reversed.

Enablement

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

It is the examiner's position that the specification is enabling for an isolated wee1 nucleic acid comprising a polynucleotide encoding SEQ ID NO:2 and a polynucleotide comprising SEQ ID NO:1, but does not reasonably provide enablement for a wee1 polynucleotide having 80% identity to the coding region of SEQ ID NO:1. Answer, page 6.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention, Raytheon Co. v. Roper Corp., 724 F.2d 951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983), and is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L. Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983). Nothing more than objective enablement is required, and therefore it is irrelevant

whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F.2d 162, 192 USPQ 29 (CCPA 1976).

The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. "Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." (footnote

omitted). In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988).

In the present case the examiner provided an analysis of several of the relevant enablement factors on pages 5-9 of the Answer. One of the examiner's primary arguments is that the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. Answer, page 7. The examiner also argues that the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in an alteration of the plant's phenotype." Id.

The examiner relies on Hemerly to support the position that the transformation of plant material is unpredictable in view of the disclosure. According to the examiner, Hemerly teaches "the transformation of *Arabidopsis* and tobacco plants with isolated nucleic acids encoding wild-type and mutant Cdc2a cell cycle regulatory proteins". Answer, page 8. Transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant designed to accelerate the cell cycle unexpectedly did not affect the development of transgenic plants. The transformation of *Arabidopsis* and tobacco with a Cdc2a mutant designed to arrest the cell cycle did affect the development of transgenic plants as expected. Id.

The examiner concludes (Id., pages 8-9)

> Given the unpredictability of determining the function of isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the unpredictability of altering the phenotype of a plant by transforming it with an isolated nucleic acid of SEQ ID NO:1 or isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the absence of guidance in the specification for making and using said nucleic acids and transgenic host cells, plants, and seeds, the lack of working examples, and given the breadth of the claims which encompass multiple polynucleotides having at least 80% identity to the entire coding region of SEQ ID NO:1, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Analysis of the enablement requirement in the present case dovetails with our analysis with respect to the written description requirement. In particular, the specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Brief, page 9. In addition, the specification page 3, lines 17-31, "describes the level of skill in the art as well as indicating areas of the wee1 gene that can be altered without disturbing substrate recognition." Brief, page 7. Moreover, the specification, page 3, states, "Most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. The carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis."

We agree with appellants that the examiner has not established that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to enable a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

Nor has the examiner established that one of ordinary skill in the art having the chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1 and the ability to test for expression as described in the specification, would be insufficient to transform cells, plants and seeds in view of the success described in the specification. While the examiner relies on Hemerly for the transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant, the examiner has not explained how or why potential unpredictability associated with Cdc2a expression is related to or affects Wee1 expression. Nor is it clear from the examiner's analysis that the examiner has fully considered the state of the art as it relates to the transformation of vectors, seeds and plant cells, as outlined in the specification.

The Patent and Trademark Office Board of Appeals stated:

> The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

In our view, upon reading the disclosure, those of ordinary skill in the art would have been provided a reasonable amount of guidance to make and use a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. The specification, pages 27-29 outlines methods for transfection and transformation of cells and the introduction of DNA into plants. The examples of the specification indicate successful expression of zmwee1 in E. coli as evidenced by the successful inhibition of cyclin-dependent protein kinase. Specification, pages 33-34. In view of the successful transformation of cells with the disclosed and claimed specific wee1, we find no evidence or sufficient indicated reason of record why one of ordinary skill in the art would not have had a reasonable expectation of success in transforming cells and plant cells with a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 without undue experimentation.

The rejection of the claims for lack of enablement is reversed.

CONCLUSION

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention is reversed.

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph for lack of enablement is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

WILLIAM F. SMITH Administrative Patent Judge	)
DEMETRA J. MILLS Administrative Patent Judge	) APPEALS AND
ERIC GRIMES Administrative Patent Judge	) INTERFERENCES

Appeal No. 2003-1993
Application No. 09/470,526

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